doi:10.1246/cl.2010.1285

Nanoaggregate Formation of Amphiphilic Alternating and Random Copolyimides in Water

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Amphiphilic alternating/random copolyimides (coPIs) formed nanoaggregates in water. The diameter of the aggregates were ca. 90 nm for the alternating coPIs and 35 nm for the random coPI. The difference in the aggregate-forming behavior was attributed to the difference in the mode of association of hydrophobic units.

Amphiphilic polymers are of interest because of their potential applicability to materials/biological fields.[1] They undergo self-association in aqueous solutions through intra- or interchain hydrophobic interactions to give aggregates such as micelles, vesicles, and cylinders.[2] Among the amphiphilic polymers, block copolymers consisting of hydrophilic and hydrophobic units have been extensively studied to date, and considerable knowledge about the structure–property relationship concerning the aggregate-forming behavior of them has accumulated.[3]

Meanwhile, there are some other types of copolymers such as random or alternating copolymers. This situation raises a question, namely, what is the effect of the distribution of hydrophilic/hydrophobic monomer units in one copolymer chain on the aggregate-forming behavior? Concerning this problem, several groups have reported the comparison of amphiphilic random or gradient copolymers with block copolymers.[4] On the other hand, Morishima et al. reported on the difference in the fluorescence behavior of amphiphilic alternating/random copolymers with luminescent probes on their side chains,[5] however, the aggregate formation of them was not referred to. Additional study is required in order to clarify the structure–property relationship of alternating copolymers.

Recently, we have succeeded in preparing alternating copolyimides (coPIs) in one pot based on the unique regioselective reactivity of a nonsymmetric spiroalicyclic dianhydride, *rel*[1*R*,5*S*,6*R*]-3-oxabicyclo[3.2.1]octane-2,4-dione-6-spiro-3′-(tetrahydrofuran-2′,5′-dione) (**DAn**).[6] It was also found that, by simply changing the experimental procedure, the corresponding random coPI could be obtained. These findings motivated us to investigate the association behavior of constitutionally isomeric amphiphilic coPIs.

In this communication, we report on the first example for the formation of nanoaggregates of amphiphilic alternating copolymer having hydrophilic/hydrophobic parts in the main chain.

We employed 1,9-bis(4-aminophenoxy)nonane as a hydrophobic diamine and tetra(ethylene glycol) bis(4-aminophenyl) ether as a hydrophilic diamine.[7] Two kinds of amphiphilic alternating coPIs, **coPI1** and **coPI2**, and the corresponding random coPI, **coPI3**, were prepared from **DAn** and the above diamines according to a procedure reported in our previous study (Figure 1).[6b] The degree of imidization for the three coPIs was estimated to be >95% on the basis of ^{1}H NMR spectroscopic measurement. The molecular weights of the three coPIs were similar, which is advantageous in comparing their aggregating behavior.

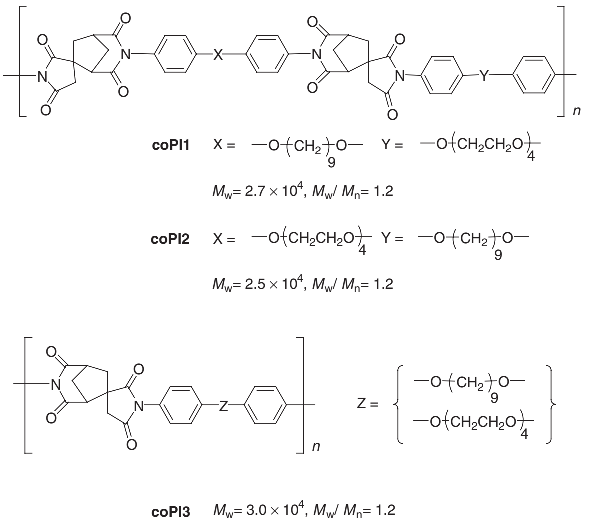

Figure 1. Structure of coPIs.

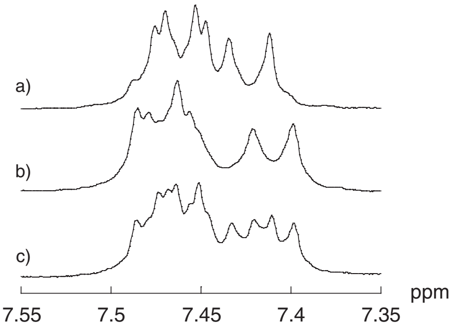

Figure 2. Part of the ^{1}H NMR data of coPAAs corresponding to a) **coPI1**, b) **coPI2**, and c) **coPI3** in DMSO-d_6.

The chemical structure of the coPIs was indirectly analyzed through the comparison of the ^{1}H NMR spectra of the copoly(amide acid)s (coPAAs), synthetic precursors of the coPIs.[6b] There was a distinct difference in the aromatic region of their ^{1}H NMR spectra (Figure 2). The spectra of the coPAAs corresponding to **coPI1** and **coPI2** were complementary to each other. The spectrum of coPAA related to **coPI3** was essentially equal to the superimposition of the above two. From these observations, we concluded that **coPI3** has random structure whereas **coPI1** and **coPI2** have ordered, alternating structure. Comparison of the ^{1}H NMR spectra of coPIs was less informative due to condsiderable overlapping of the signals.

The coPIs were subjected to the following aggregate-forming process: coPIs were first dissolved in *N*,*N*-dimethylform-

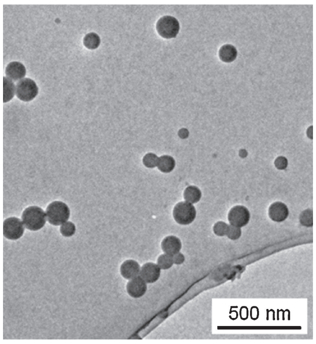

Figure 3. TEM image of **coPI1** nanoaggregates from **coPI1** in water.

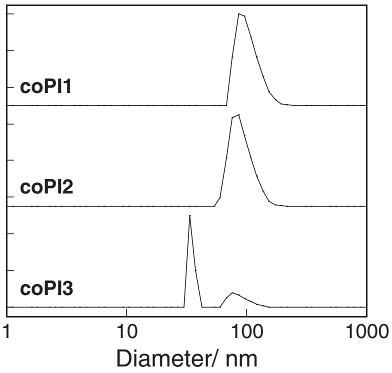

Figure 4. D_H of the aggregates derived from coPIs at a concentration of 0.2 mg mL^{-1}.

amide (DMF), then deionized water was slowly added to the solution, and the DMF–water solution was dialyzed against water to remove DMF.

The solutions of **coPI1** and **coPI2** were slightly turbid at the concentration of 0.2 mg mL^{-1}. In contrast, the solution of **coPI3** was optically clear at the same concentration. In order to evaluate formation of aggregates, a dried sample of **coPI1** solution was analyzed by transmission electron microscopy (TEM) (Figure 3). Spherical particles with a diameter mostly in the range of 70 to 140 nm were observed, and an average size of them was calculated to be 98 nm. Next, dynamic light scattering (DLS) measurement of the same **coPI1** solution was performed. The results indicated the formation of particles of monodispersed size distribution with the averaged hydrodynamic diameter (D_H) of 92 nm (Figure 4). This size was in good agreement with the diameter for the nanoparticles observed in TEM.

Formation of nanoaggregates was also confirmed for the dialyzed solution of **coPI2**, another alternating coPI having a molecular structure of which the hydrophilic and the hydrophobic components are swapped compared to **coPI1**. The averaged D_H of **coPI2** measured by DLS was 86 nm, and this value was quite similar to that of **coPI1**. This indicates that, for these two coPIs having structural regularity, the nanoaggregate forming behavior is controlled by the alternating nature of the hydrophilic and hydrophobic components, and less governed by the precise structure of the whole macromolecule.

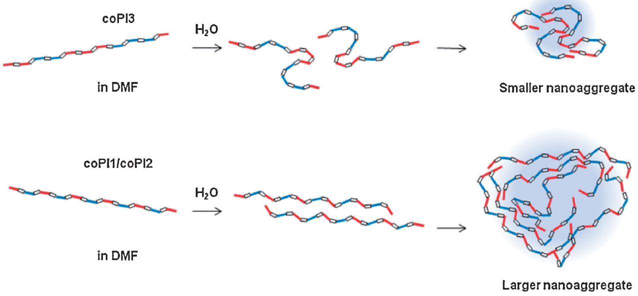

Figure 5. Schematic representation of formation of nanoaggregates of coPIs having different structural regularity (blue parts: tetraethyleneoxy, red parts: nonylene).

In contrast, DLS experiment of the random **coPI3** gave a bimodal particle size distribution with D_H values of 35 and 81 nm (Figure 4). The difference in the size of aggregates for **coPI1** and **coPI3** was also confirmed by scanning electron microscope (SEM) (Figure S1).[8]

In the course of preparation of the aggregates in the present system, the coPIs are considered to be unimolecularly dissolved in the DMF before the addition of water on the basis of the absence of the peak in the DLS measurement of the DMF solution. When water is added to the DMF solution, the solvent becomes progressively worse for the hydrophobic units including nonylene groups. At a certain water content, the nearby hydrophobic parts in the **coPI3** chain might start to associate intramolecularly to result in the formation of a hydrophobic domain, and such macromolecules should gather in order to minimize the unfavorable contact of the hydrophobes to water, resulting in the formation of nanoparticles having fairly compact hydrophobic cores (Figure 5). In the case of **coPI1** and **coPI2**, the intramolecular hydrophobe association should be effectively prevented due to the alternating nature of the polymer chain. Instead, they might form molecular aggregates based on intermolecular hydrophobic interactions, and the size of such an aggregate should be larger because of the looser packing of the hydrophobes. The bimodal nature for the D_H value of **coPI3** might indicate that some of these random coPI molecules undergo intermolecular-mode association like those of **coPI1** and **coPI2**.

In summary, a new class of amphiphilic alternating copolymer having hydrophilic and hydrophobic portions alternately in the main chain was demonstrated. Interestingly, the size and distribution of PI particles from alternating and random coPIs were different, which gives a new insight to the sequence effect on the association behavior of amphiphilic copolymers. Further study on amphiphilic polyimides including the application to materials is now under way in this laboratory.

The authors thank Profs. Masahiko Abe, Hideki Sakai, and Dr. Koji Tsuchiya at Tokyo University of Science for the use of DLS instrument and their kind help in TEM measurements. This work was financially supported by a Grant-in-Aid for Scientific Research (No. 17550113) from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

References and Notes

1 G. S. Kwon, K. Kataoka, *Adv. Drug Delivery Rev.* **1995**, *16*, 295; K. Kataoka, A. Harada, Y. Nagasaki, *Adv. Drug Delivery Rev.* **2001**, *47*, 113; A. Lavasanifar, J. Samnel, G. S.

Kwon, *Adv. Drug Delivery Rev.* **2002**, *54*, 169; R. Haag, *Angew. Chem., Int. Ed.* **2004**, *43*, 278.

2 L. Zhang, A. Eisenberg, *Science* **1995**, *268*, 1728; J. C. M. V. Hest, D. A. P. Delnoye, M. W. P. L. Baars, M. H. P. V. Genderen, E. W. Meijer, *Science* **1995**, *268*, 1592; J. J. L. M. Cornelissen, M. Fischer, N. A. J. M. Sommerdijk, R. J. M. Nolte, *Science* **1998**, *280*, 1427; D. E. Discher, A. Eisenberg, *Science* **2002**, *297*, 967; R. C. Claussen, B. M. Rabatic, S. I. Stupp, *J. Am. Chem. Soc.* **2003**, *125*, 12680; D. Yan, Y. Zhou, J. Hou, *Science* **2004**, *303*, 65.

3 A. Blanazs, S. P. Armes, A. J. Ryan, *Macromol. Rapid Commun.* **2009**, *30*, 267; *Amphiphilic Block Copolymers: Self-Assembly and Application*, ed. by P. Alexandridis, B. Lindman, Elsevier Science B. V., Amsterdam, **2000**, and references cited therein.

4 Y. Chang, C. L. McCormick, *Macromolecules* **1993**, *26*, 6121; P. Hodrokoukes, S. Pispas, N. Hadjichristidis, *Macromolecules* **2002**, *35*, 834; S. Okabe, K. Seno, S. Kanaoka, S. Aoshima, M. Shibayama, *Macromolecules* **2006**, *39*, 1592; R. C. W. Liu, A. Pallier, M. Brestaz, N. Pantoustier, C. Tribet, *Macromolecules* **2007**, *40*, 4276; T. B. Bonné, K. Lüdtke, R. Jordan, C. M. Papadakis, *Macromol. Chem. Phys.* **2007**, *208*, 1402; R. Hoogenboom, H. M. L. Thijs, D. Wouters, S. Hoeppener, U. S. Schubert, *Macromolecules* **2008**, *41*, 1581; M. Barz, R. Luxenhofer, R. Zentel, A. V. Kabanov, *Biomaterials* **2009**, *30*, 5682.

5 Y. Morishima, T. Kobayashi, S. Nozakura, S. E. Webber, *Macromolecules* **1987**, *20*, 807.

6 a) J. Li, J. Kato, K. Kudo, S. Shiraishi, *Macromol. Chem. Phys.* **2000**, *201*, 2289. b) K. Kudo, T. Yoshizawa, T. Hamada, J. Li, S. Sakamoto, S. Shiraishi, *Macromol. Rapid Commun.* **2006**, *27*, 1430.

7 A. Shiotani, M. Kohda, *J. Appl. Polym. Sci.* **1999**, *74*, 2404; J. M. García, J. G. D. L. Campa, G. Schwarz, J. D. Abajo, *Macromol. Chem. Phys.* **2001**, *202*, 1298.

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